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(54) Title: TUBULAR DEVICE WITH HYDROPHILIC SURFACE

(57) Abstract

The invention relates to a tubular device (other than a Foley balloon catheter for urine drainage purposes) for supplying fluid (gas or liquid) to, or removing fluid from, the body of a patient. According to the invention the tubular device comprises an elongate tubular body having one end for insertion in the body of a patient wherein at least over a portion of its length extending from the insertion end the exposed surface of the body is of a polyurethane and over said length the body is provided with a coating of poly(N-mono hydroxy)propyl methacrylamide) bonded to said polyurethane surface by residues of a di or higher functionality isocyanate compound.

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TUBULAR DEVICE WITH HYDROPHILIC SURFACE

The present invention relates to a tubular device (other than a Foley balloon catheter for urine drainage purposes) for supplying fluid (gas or liquid) to, or removing fluid from, the body of a patient.

Examples of tubular devices with which the present invention is concerned include catheters (eg. cardiovascular catheters and radiological catheters), and anaesthesia tubes (eg. endotrachial tubes). For convenience, all such devices are referred to herein as catheters.

To facilitate insertion and withdrawal of a catheter into the body, it is desirable that the catheter have (over at least that part of its length which is inserted in the body) a surface which has a low-coefficient of friction when in contact with aqueous body fluids. In other words, the wetted surface should feel "slippery". Such a surface also minimises rubbing between the catheter and the body of the patient during residence of the catheter in the body and therefore minimises discomfort to the patient.

According to a first aspect of the present invention there is provided a catheter other than a Foley balloon catheter comprising an elongate tubular body having one end for insertion in the body of a patient wherein at least over a portion of its length extending from the insertion end the exposed surface of the body is of a polyurethane and over said length the body is provided with a coating of poly(N-(mono hydroxy)propyl methacrylamide) bonded to said polyurethane surface by residues of a di or higher functionality isocyanate compound.

According to a second aspect of the present invention there is provided a method of producing a catheter as defined in the preceding paragraph comprising treating said exposed surface with a di or higher functionality isocyanate compound and with poly(N-(mono hydroxy)propyl methacrylamide) so that the latter is bonded to said surface by residues of the di or higher functionality isocyanate compound to form a coating on the surface.

Preferably the poly(N-(mono hydroxy)propyl methacrylamide) is poly(N-(2-hydroxy)propyl methacrylamide), although other isomers in which the hydroxy group is at a different position on the propyl chain may be used. The invention will be specifically described with respect to poly(N-(2-hydroxy)propyl methacrylamide) although the following

description is applicable mutatis mutandis to the other isomers.

The poly(N-(2-hydroxy)propyl methacrylamide) (hereinafter referred to simply as HPMA) provides a coating which is a "glassy material" when dry and a hydrogel when wetted with aqueous body fluids. Upon wetting, the HPMA provides the necessary low friction coating which facilitates insertion and withdrawal of the catheter and prevents damage from "rubbing" between the catheter and the body of the patient.

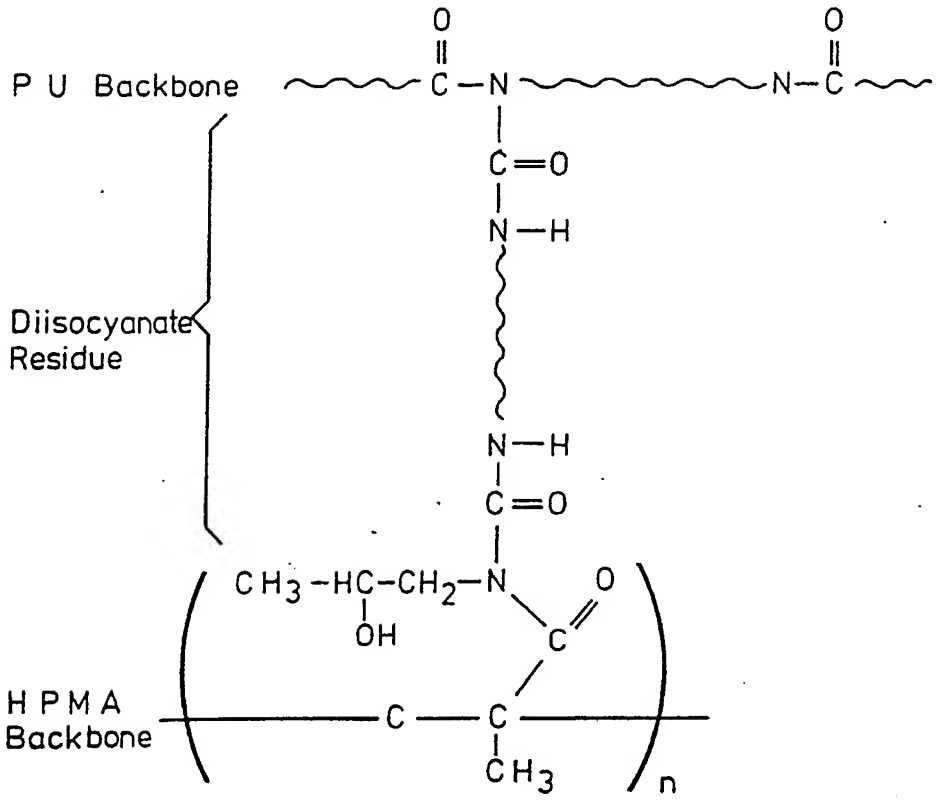
The HPMA provides several advantages. In particular, the wetted HPMA provides low friction for insertion and low mechanical trauma to biological tissue. Additional advantages are better blood, urine and tissue compatibility as well as reduction of infection rates.

Preferably the HPMA has a molecular weight (M_w) of at least 20,000 daltons as measured by GPC using polystyrene standard calibration. The preferred M_w range is 50,000-150,000 daltons. Preferably, the HPMA is a homopolymer although comonomers can be included, preferably in an amount less than 10% by mole, more preferably less than 2% by mole. A preferred such comonomer is methacrylic acid.

Preferably the body of the catheter is of polyurethane, e.g. Estane (Goodrich), Pellethane (Dow) or Elastolan (BASF). It is however within the scope of the invention for the body of the catheter to be of a different material which is coated with a polyurethane.

The HPMA is bonded to the polyurethane surface of the body by means of residues of a di or higher functionality isocyanate compound. This isocyanate compound may be aliphatic, aromatic or alicyclic. Examples of suitable isocyanates are aliphatic diisocyanates having 3 to 10 carbon atoms, more preferably 5 to 7 carbon atoms. A preferred aliphatic diisocyanate is hexamethylene diisocyanate (HDI). Of the aromatic isocyanates which may be used, the preferred compound is pure HMDI.

The bonding of the HPMA coating to a polyurethane surface is illustrated somewhat schematically below.



Although the above illustration shows the isocyanate residue being bonded to a nitrogen atom of the HPMA, it is also possible it is bonded to a carbon atom.

The HPMA coating may be applied to the polyurethane surface of the catheter body in a number of ways, examples of which are given below.

In one method, a solution of the isocyanate (eg. MDI) and HPMA is formulated in a suitable solvent. Typically the concentration of the diisocyanate in the solution will be in the range 0.5-5% whereas the concentration of the HPMA will generally be 1-5%. Suitable solvents

include dimethyl formamide (DMF) as well as mixtures of DMF with lower boiling solvents eg. tetrahydrofuran or methyl ethyl ketone. DMAC, DMSO and NMP may also be used.

That length of the catheter which is to be provided with the HPMA coating is dipped into the abovedescribed solution, typically for a time of less than 10 seconds. After this dipping process, the catheter is "dried" to leave the surface coating of HPMA bonded to the polyurethane by isocyanate compound residues. Typically the drying condition includes IR drying (eg. 4-8 mins at 65-70°C) followed by drying (in a fan oven) for several hours at 50-70°C, (e.g. 3-8 hrs at 60°C).

In an alternative method of applying the HPMA coating, the length of the catheter is initially dipped into a solution of the isocyanate (the isocyanate solution) so that isocyanate compound residues become bonded to the polyurethane, followed by dipping into a solution of the HPMA (the HPMA solution), preferably containing a catalyst for forming polyurethanes.

The solvent for the isocyanate solution is preferably a halocarbon, preferably one containing chlorine and/or fluorine. Preferred examples of such solvents are low boiling liquids such as methylene chloride, chloroform etc.

The concentration of the isocyanate is preferably 1-5%. The dipping time of the catheter in the isocyanate solution is preferably less than 10 seconds.

After this dipping process, the catheter is removed from the solution and the solvent is allowed to evaporate in air prior to the catheter being dipped in the HPMA solution containing a polyurethane formation catalyst. A suitable concentration range for the HPMA is 0.5-5% and the preferred solvent is a mixture of DMF (50-75%) and THF (25-50%) Other solvents which can be used include DMAC, DMSO, and NMP. The polyurethane formation catalyst is preferably used in an amount of 1 part of catalyst per 500-10000 parts of HPMA. The catalyst may for example be stannous octoate, stannous chloride, diethyl zinc, diphenyl zinc, and other common organometallic catalysts used in

polyurethane formation reactions. This dipping process is preferably effected for less than 10 seconds.

Upon removal of the catheter from the HPMA solution, the catheter is dried preferably at a temperature of 65-70°C for 8-12 minutes. Finally the catheter is washed with water and dried in warm air.

As a result of the abovedescribed treatments, at least a portion of the length of the catheter has a surface of HPMA covalently bonded to the polyurethane. This covalent bonding ensures that the HPMA is firmly bonded to the catheter surface and so can repeatedly be made hydrophilic.

Catheters in accordance with the invention may be kept within the body for 10-12 weeks without problem.

If desired, the HPMA coating may include an anti-microbial agent or a drug for delivery to the body of the patient, eg. copper or silver compounds, chlorhexidine or other antiseptic, or an antibiotic.

Claims

1. Tubular device for supplying fluid to, or removing fluid from, the body of a patient comprising an elongate tubular body having one end for insertion in the body of a patient

characterized in

that at least over a portion of the length of the elongate tubular body extending from the insertion end the exposed surface of the body is of a polyurethane and over said length the body is provided with a coating of poly(N-(mono hydroxy) propyl methacrylamide) bonded to said polyurethane surface by residues of a di or higher functionality isocynate compound.

2. Tubular device according to claim 1,

characterized in

that the poly(N-(mono hydroxy)propyl methacrylamide) is poly(N-(2-hydroxy)propyl methacrylamide) or an other insomer in which the hydroxy group is at a different position on the propyl chain.

3. Method of producing a tubular device according to claim 1 or 2

characterized in

treating said exposed surface with di or higher funcitonality isocyanate compound and with poly(N-(mono hydroxy) propyl methacrylamide) so that the latter is bonded to said surface by residues of the di or higher functionality isocyanate compound to form a coating on the surface.

INTERNATIONAL SEARCH REPORT

International Application No PCT/EP 92/00919

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all)[6]

According to International Patent Classification (IPC) or to both National Classification and IPC

Int.Cl. 5 A61L29/00

II. FIELDS SEARCHED

Minimum Documentation Searched[7]

Classification System	Classification Symbols
Int.Cl. 5	A61L

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched[8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT[9]

Category °	Citation of Document, [11] with indication, where appropriate, of the relevant passages [12]	Relevant to Claim No.[13]
A	EP,A,0 166 998 (TERUMO KABUSHIKI KAISHA) 8 January 1986 see page 4, line 12 - line 25; claims	1-3
A	EP,A,0 106 004 (INTERNATIONAL SILICONE CORPORATION) 25 April 1984 see claims	1-3
A	EP,A,0 379 156 (UNION CARBIDE CHEMICALS AND PLASTICS COMPANY INC.) 25 July 1990 see examples	1-3

° Special categories of cited documents :[10]

"A" document defining the general state of the art which is not considered to be of particular relevance

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IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
04 SEPTEMBER 1992	17. 09. 92
International Searching Authority	**Signature of Authorized Officer**
EUROPEAN PATENT OFFICE	M. ESPINOSA Maria del Ros

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ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO. EP 9200919 SA 59302

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 04/09/92
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		JP-C- 1549319	09-03-90
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